

REMARKSI. Status of the claims:

Claims 1-14 are pending in this applications.

II. Rejection of claims 1-14

The examiner has rejected claims 1-14 under 35 U.S.C. § 103(a) as unpatentable over WO 96/27606 to Cook et al. ("Cook") in view of the *Nucleosides & Nucleotides* article by McGee ("McGee"). The examiner asserts that Cook teaches a process for the synthesis of 2'-O-substituted pyrimidines via reaction of the corresponding 2-2'-anhydropyrimidine nucleoside with a Lewis acid. The examiner acquiesces that Cook only specifically uses tris-O-substituted boron (i.e., B(OR)₃) and does not explicitly state that the Lewis acid can be tris-O-substituted aluminum (i.e., Al(OR)₃). However, the examiner concludes that it would have been obvious to one of ordinary skill in the art to use any one of the disclosed Lewis acids taught in Cook because Cook teaches that tri-alkyl borates are effective and McGee teaches that other Lewis acids, such as magnesium and calcium alkoxides, are also effective.

Importantly, the examiner recognizes that neither Cook nor McGee teach the conversion of a 2-2'-anhydropyrimidine nucleoside to a 2'-O-substituted pyrimidine using Al(OR)₃, as claimed by the applicants. Nor is there any disclosure in Cook or McGee that would motivate the skilled artisan to selected the process of claimed invention. It is the applicants position that it would not be obvious to use Al(OR)₃ in any of the processes disclosed in the prior art, as evidenced by the applicants showing of unexpected results.

In the Response filed on September 22, 2003, the applicants compared example 41 of Cook to an example disclosed in the applicants' specification on page 7, lines 15-25. In example 41, Cook uses tris(2-methoxyethyl) borate to achieve a yield of 63% of 2'-O-(2-methoxyethyl)uridine, while the applicants use aluminum tri(methoxyethoxide) being employed in place of the tris(2-methoxy ethyl) borate to yield 91% 2'-O-(2-methoxyethyl)uridine. The increase in yield from 63% to 91% represents an unexpected benefit of using the applicants' claimed Al(OR)₃ instead of the disclosed B(OR)₃.

In response to the applicants' assertion of unexpected benefits, the examiner notes in the January 22, 2004 official action, "Applicants' remarks concerning 'unexpected results' have been noted; however, the arguments of counsel cannot take the place of evidence in the record." Therefore, in this response, the applicants submit a declaration under 37 C.F.R. § 1.132 by Dr. Mark Edward Douglas to introduce the unexpected results into the record.

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In the declaration, Dr. Douglas compares example 41 of Cook preparing 2'-O-(2-methyl)uridine to a similar example in the applicants' specification on page 7, lines 15-25 also preparing 2'-O-(2-methyl)uridine. In the Cook example, Cook uses tris(2-methoxyethyl) borate under forcing conditions of 155° C to 160° C to achieve a yield of 63% 2'-O-(2-methyl)uridine. In contrast, the applicants use aluminum tri(methoxyethoxide) in a reaction equivalent to example 41 of Cook at a temperature of 125° C to achieve a yield of 91% 2'-O-(2-methyl)uridine. In view of this data, Dr. Douglas concludes that the yield achieved by the process claimed in the applicants' invention is surprisingly and unexpectedly high, especially in view of the substantially lower temperature employed by the applicants.

The unexpected results submitted in the declaration by Dr. Douglas provide the evidence of record requested by the examiner. Accordingly, the applicants respectfully request that the examiner withdraw the rejection under 35 U.S.C. § 103.

III. Conclusion

The applicants believe the application is in condition for allowance and respectfully request early notification to that effect. Should any issues remain unresolved, the examiner is encouraged to contact the undersigned attorney for the applicants at the telephone number indicated below in order to expeditiously resolve any remaining issues.

Respectfully submitted,

PILLSBURY WINTHROP LLP

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By:



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